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June 23, 2004

Michael O. Leavitt, Administrator
US Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Comments on the HPV test plan for Commercial Hydroxyethylpiperazine

Dear Administrator Leavitt:

The following are comments on the test plan for Commercial Hydroxyethylpiperazine (CHEP, CAS# 103-76-4) for the HPV program, submitted by The Dow Chemical Company (Dow). These comments are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These animal, health and environmental protection organizations have a combined membership of more than ten million Americans.

Dow proposes to do an OECD 421 screening protocol on this chemical, which will kill approximately 675 animals. Dow is also proposing to do a chromosomal aberration test, using OECD protocol 473.

CHEP is a commercial preparation that consists of varying concentrations of four chemicals: Hydroxyethylpiperazine (CAS# 103-76-4), bis-Dihydroxyethylpiperazine (CAS# 122-96-3), Piperazine (CAS# 110-85-0), and water (CAS# 7732-18-5). Although there are no data available for this closed-system intermediate chemical mixture, there are some data available for some components to fulfill most endpoints required by the HPV program. Since the chemical is a CSI, the only required mammalian toxicity endpoints under the HPV program are chromosomal aberration and developmental toxicity. However, there are compelling reasons that animal life need not be sacrificed at all in this case.

First, we want to ensure that Dow uses either human lymphocytes or mammalian cells obtained from established cultures for its proposed OECD 473, so as to avoid killing additional animals in order to supply the cells.

Second, we request that Dow consider whether useful information would result from the proposed OECD 421. Since CHEP is a known dermal irritant and sensitizer, the proposed test via dermal exposure is likely to produce additional stress in the pregnant animals. It has been reported in the developmental toxicology literature that maternal stress may be related to developmental effects, and so it would be difficult to imply causation in the event of a positive result. Further, Dow states in the test plan that there

are only small numbers of workers exposed (the public is not likely to be exposed), and they already wear protective equipment, including air respirators, monogoggles, gloves, and other protective clothing, because of the dermal irritation and sensitization potential of this mixture. Since a component of the mixture (piperazine) has yielded a positive result in a 2-generation reproductive study, regulation to account for that result will similarly limit exposure in target groups, if in fact a positive result occurs.

The EPA has clearly stated, "In analyzing the adequacy of existing data, participants shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach. Participants may conclude that there is sufficient data, given the totality of what is known about a chemical, including human experience, that **certain endpoints need not be tested**" and "as with all chemicals, before generating new information, participants should further consider whether any additional information obtained would be useful or relevant" (see *http://www.epa.gov/chemrtk/ceoltr2.htm*).

Thank you for your attention to this issue. I look forward to a prompt and favorable response to our concerns. I can be reached at 202-686-2210 ext. 335 or via email at *kstoick@pcrm.org*.

Sincerely,

Kristie Stoick, MPH
Research Analyst

Chad B. Sandusky, PhD
Director of Research